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The prognostic molecular markers in hepatocellular carcinoma.

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The prognosis of hepatocellular carcinoma (HCC) still remains dismal, although many advances in its clinical study have been made. It is important for tumor control to identify the factors that predispose patients to death. With new discoveries in cancer biology, the pathological and biological prognostic factors of HCC have been studied quite extensively. Analyzing molecular markers (biomarkers) with prognostic significance is a complementary method. A large number of molecular factors have been shown to associate with the invasiveness of HCC, and have potential prognostic significance. One important aspect is the analysis of molecular markers for the cellular malignancy phenotype. These include alterations in DNA ploidy, cellular proliferation markers (PCNA, Ki-67, Mcm2, MIB1, MIA, and CSE1L/CAS protein), nuclear morphology, the p53 gene and its related molecule MD M2, other cell cycle regulators (cyclin A, cyclin D, cyclin E, cdc2, p27, p73), oncogenes and their receptors (such as ras, c-myc, c-fms, HGF, c-met, and erb-B receptor family members), apoptosis related factors (Fas and FasL), as well as telomerase activity. Another important aspect is the analysis of molecular markers involved in the process of cancer invasion and metastasis. Adhesion molecules (E-cadherin, catenins, serum intercellular adhesion molecule-1, CD44 variants), proteinases involved in the degradation of extracellular matrix (MMP-2, MMP-9, uPA, uPAR, PAI), as well as other molecules have been regarded as biomarkers for the malignant phenotype of HCC, and are related to prognosis and therapeutic outcomes. Tumor angiogenesis is critical to both the growth and metastasis of cancers including HCC, and has drawn much attention in recent years. Many angiogenesis-related markers, such as vascular endothelial growth factor (VEGF), basic fibroblast growth factor (bFGF), platelet-derived endothelial cell growth factor (PD-ECGF), thrombospondin (TSP), angiogenin, pleiotrophin, and endostatin (ES) levels, as well as intratumor microvessel density (MVD) have been evaluated and found to be of

prognostic significance. Body fluid (particularly blood and urinary) testing for biomarkers is easily accessible and useful in clinical patients. The prognostic significance of circulating DNA in plasma or serum, and its genetic alterations in HCC are other important trends. More attention should be paid to these two areas in future. As the progress of the human genome project advances, so does a clearer understanding of tumor biology, and more and more new prognostic markers with high sensitivity and specificity will be found and used in clinical assays. However, the combination of some items, i.e., the pathological features and some biomarkers mentioned above, seems to be more practical for now.

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